WHAT IS CLAIMED IS:

1. A method for reducing inducement of histopathological change in a target muscle tissue site resulting from application of an electric field to a subject to deliver a therapeutic agent thereto, said method comprising:

introducing an effective amount of at least one therapeutic agent into the target muscle tissue site of a subject;

generating an electric field at the target muscle tissue site of the subject by introducing from 1 to about 4 monopolar DC pulses, each pulse having a duration of about 10 ms to about 100 ms, to generate a nominal field strength of about 100V/cm to about 300V/cm at the target muscle tissue site,

thereby reducing the inducement of histopathological change in the target muscle tissue site resulting from application of the electric field as compared to alternative methods for applying an electric field to the target muscle tissue site.

2. The method of claim 1, wherein the histopathological change is associated with the induction or amplification of an immune response.

3. The method of claim 1, wherein the histopathological change is inflammation.

4. The method of claim 1, wherein the histopathological change is necrosis.

5. The method of claim 1, wherein the histopathological change is fibrosis.

6. The method of claim 1, wherein the duration of each pulse is in the range from about 20 ms to about 60 ms.

7. The method of claim 1, wherein there are no more than two pulses at each target muscle tissue site.

8. The method of claim 1, wherein the nominal field strength is in the range from about 100 V/cm to about 232 V/cm.

9. The method of claim 8, wherein the nominal field strength is in the range from about 100 V/cm to about 150 V/cm.

10. The method of claim 8, wherein the duration of each pulse is in the range from about 40 ms to about 60 ms.

11. The method of claim 1, wherein the electric field is generated by applying to the subject electroporation electrodes, wherein a portion of the electrodes that contacts the subject is made of a non-toxic, biocompatible metal.

12. The method of claim 11, wherein the metal is gold.

13. The method of claim 1, wherein the subject is a mammal.

14. The method of claim 1, wherein the subject is a human.

15. An *in vivo* method for enhancing expression of a therapeutic polypeptide encoded by a isolated polynucleotide to be delivered into cells in a subject, said method comprising:

a) introducing an effective amount of at least one isolated polynucleotide encoding a therapeutic polypeptide into a target muscle tissue site of a subject; and

b) generating an electric field at the target muscle tissue site by introducing from 1 to about 4 monopolar DC pulses, each having a pulse duration of about 10 to about 100 ms, to generate a nominal field strength of about 100V/cm to about 300V/cm at the target muscle tissue site, at substantially the same time as the introduction of the polynucleotide so as to result in the polynucleotide entering cells of the target muscle tissue for expression of the therapeutic polypeptide therein;

thereby enhancing the expression of the therapeutic polypeptide as compared to expression of the therapeutic polypeptide achieved by other methods for generating an electric field in the target muscle tissue.

16. The method of claim 15, wherein the histopathological change is associated with the induction or amplification of an immune response.

17. The method of claim 15, wherein the histopathological change is inflammation.

18. The method of claim 15, wherein the duration is in the range from about 20 ms to about 60 ms.

19. The method of claim 15, wherein there are no more than two pulses.

20. The method of claim 15, wherein the nominal field strength is in the range from about 100 V to about 150 V.

21. The method of claim 33, wherein the duration of the pulses is in the range from about 40 ms to about 60 ms.

22. The method of claim 33, wherein the electric field is generated by applying to the subject electroporation electrodes, wherein a portion of the electrodes that contacts the subject is made of a non-toxic, biocompatible metal.

23. The method of claim 36, wherein the metal is gold.

24. The method of claim 35, wherein the subject is a mammal.

25. The method of claim 15, wherein the subject is a human.

26. The method of claim 15, wherein the polynucleotide is injected intramuscularly at from 1 to about 20 sites in the target muscle tissue.

27. The method of claim 15, wherein said polynucleotide is selected from the group consisting of double stranded DNA, single-stranded DNA, complexed DNA, formulated DNA, encapsulated DNA, naked RNA, encapsulated RNA, and combinations thereof.

28. The method of claim 15, wherein the polynucleotide encoding the therapeutic polynucleotide is contained in a DNA vector.

29. The method of claim 15, said polynucleotide being operably associated with a regulatory sequence for expression of the therapeutic polypeptide in said cells.

30. The method of claim 15, wherein said polynucleotide further encodes a selectable marker polypeptide.

31. The method of claim 29, wherein said regulatory sequence comprises a promoter.

32. The method of claim 31, wherein said promoter is muscle specific.

33. The method of claim 32, wherein said promoter is selected from CMV, RSV LTR, MPSV LTR, and SV40 promoters.

34. The method of claim 15, wherein the electric pulses are administered to the target muscle tissue using an electroporation electrode comprising a plurality of electrically conducting needles.

35. The method of claim 34, wherein a portion of the needles that contacts the subject is made of a non-toxic, biocompatible metal.

36. The method of claim 35, wherein the metal is gold.

37. A method for delivering a polynucleotide encoding a polypeptide to a target muscle tissue site comprising:

a) introducing an effective amount of at least one isolated polynucleotide encoding a polypeptide into a target muscle tissue site of a subject;

b) introducing at least a conductive portion of an electrode needle array into the target muscle tissue site; and

c) applying from 1 to about 4 monopolar DC pulses having a duration of about 10 ms to about 100 ms each to generate a nominal field strength of about 100V/cm to about 300V/cm at the target muscle site;

thereby delivering the polynucleotide to the target muscle.

38. The method of claim 37, wherein the electrode needle array comprises four electrode needles and two pulses are applied to the target muscle tissue site to generate a nominal field strength of about 116 V/cm.